Evidence Report Disposition of Comments Report

Research Review Title: *Health Information Exchange*

Draft review available for public comment from March 12 to April 8, 2015.

Research Review Citation: Hersh W, Totten A, Eden K, Devine B, Gorman P, Kassakian S, Woods S, Daeges M, Pappas M, McDonagh M. Health Information Exchange. Evidence Report/Technology Assessment No. 220. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2012-00014-I.) AHRQ Publication No. 15(16)-E002-EF. Rockville, MD: Agency for Healthcare Research and Quality; December 2015. www.effectivehealthcare.ahrq.gov.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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Published Online: December 15, 2015

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #1	Executive Summary	ES Page 12 Ln 18 (and in abstract) This statement “answered the question in limited ways” is a little loaded and potentially misleading to lay readers. The idea is also in the abstract pg 7 ln 5. From the context, it appears the authors not talking about the strength of the design or study limitations, but are talking about the number of outcomes that have been studied. That is accurate, because the number of potential effects of HIE (from the literature) is assumed to be pretty broad. However, that label limited doesn’t really reflect the challenges or realities of research. I would not want to reader who sees that an evaluation “only” studied the effects of HIE on A1C values as limited because it only included one condition/one use case. That isn’t a limitation, but more of a reality that no study can study everything possible. If the authors want to say only a few different outcomes have been considered, that it fine and accurate. But to label them as limited and then in the next sentences to talk about limitations in designs (which are there are too) gives the wrong idea.	We disagree that "limited" means just one or a small number of factors studied. Instead, we call the studies limited by the narrow and retrospective nature of the questions assessed. We clarify this in that section of the text now.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #1	Executive Summary	ES Page 13 Ln 31-44 The authors might want to qualify these findings by the type of HIE (portal/query or automated/push). It is a little tricky in this section. The overall statistics on usage in the above paragraphs do not make such distinctions. However, the actual statistics on usage in this specific section is only on portals, which have very different usage rates than push. Also, these rates of usage are old.	Thank you for your suggestion. The distinction between portal/query and automated/push HIEs is made in the Results section for Key Question #4, in the main body of the report. Specifically, in the in-text table, for each study wherein is specified the type of HIE (query/push), we have so designated. For studies that include several HIEs from wider geographic areas, the type of HIE is not specified in the study; in these instances we use the term 'varies'. Throughout the Results section of Key Question #4, we have paid particular attention to study chronology, and trends in increased usage over time. We agree that some of these studies, particularly those that describe within state HIEs are now older. Had more recent data been available, we would have also included it. Perhaps more informative are the more recent usage rates that are available from the national surveys, which we also include.
TEP Reviewer #1	Executive Summary	ES page 15 Ln 30 to Page 16 Conclusions One of the challenges or important context pieces not addressed in the ES is the maturity of HIE efforts and the number of operational activities in place. It would take a careful or knowledgeable reader to realize that the ES section on adoption reported that adoption was low prior to ARRA (2009), but much of the research results are about from studies pre-dating this time or more often using systems that were developed prior to 2009. The ES does not convey there is a period of time, measured in multiple years, between adoption of HIE and sufficient levels of system maturity (enough users, data, etc) to conduct research.	We now note that HIE is relatively immature.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #2	Executive Summary	For Table ES-1, Please split the table into sections by topic. The number of included studies by type should be it's own column. The current version has a very jumbled presentation in the first column.	This is a good idea, and we have done this in the ES as well as Discussion section of the main report.
Peer Reviewer #3	Executive Summary	In the Executive Summary, the statement: "The HITECH Act designated an additional $564 million for investment in state-level HIE." This makes it sound like the ONC Grant program was to develop statewide HIEs, which it wasn't. The goal was for states to develop an infrastructure for statewide exchange but could use a variety of methods, including supporting multiple exchange activities within a state, encourage commercial HIEs, encourage Direct HISPs to compete in the state, etc.	We have clarified here and in the Introduction section of the main report that the HITECH Act provided funding for state-designated entities to develop HIE.
TEP Reviewer #4	Executive Summary	Page ES-3 line 22 few or fewer	We have fixed this to be "fewer."
TEP Reviewer #4	Executive Summary	Page ES-3 Line 32 the statement regarding medication adherence not improving during the study is difficult to interpret without further information.	We have clarified the outcomes in the medication adherence study of reference 21.
TEP Reviewer #4	Executive Summary	Page ES-3 Line 40 The statement relating to the study of HIE providing pharmacy information in the ED is interesting, but the information here is so summarised that it is difficult to interpret. E.g As this information is provided under the broad topic of 'perceptions' – did this study only report physicians' perceptions of time taken to provide ED care (is this what is meant by service here?)	We have clarified the results of the study of providing HIE information about pharmacy in the ED (Kaushal).
TEP Reviewer #4	Executive Summary	ES-5 This section describes studies reporting barriers and facilitators to implementation of HIE. As I read through this section I wondered whether all these studies focused on implementation or in fact 'use' of HIE. For example line 56 describes "HIE designs that reflected workflow and included functions that could be integrated into care process" as a facilitator of implementation, but these seem clearly to be more associated with potential facilitators for use once implemented. Thus I wondered whether these different concepts should be distinguished. These issues are more clearly teased out in the main body of the review.	We have updated the ES to clarify which part is barrier to actual use.

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TEP Reviewer #4	Executive Summary	ES-6 Line 5. It is not clear what is meant by 'grants' in this context. Do you mean research grants or grants to support implementation of HIE e.g. by government funding agencies. It is not directly apparent how a grant would facilitate use of an HIE. Ie grants would seem to facilitate the implementation of an HIE.	The text has been revised to clarify that this refers to grants that supported the implementation of HIE.
TEP Reviewer #4	Executive Summary	Page ES-6 line 17 includes ..user interface and functionality- once again these would seem to have more to do with barriers to use rather than to implementation.	The text has been revised to clarify that the barrier is the lack of resources necessary to address interface and function issues. Not having these resources is a barrier to implementation.
TEP Reviewer #4	Executive Summary	Implications and Conclusions ES-7 These sections provide a very useful summary and highlights the limitations of the evidence base. I wondered whether a little more attention might be placed on specifically outlining the type of research required. While the authors call for research using more robust study designs, and building on existing research it would be useful for the authors, who have reviewed such as vast body of research to be more specific about the type and design of research that they believe will move the agenda forward. I anticipate that many readers seeking the answers from this review would be challenged to identify the type of research that is required to more comprehensively identify how HIE can contribute to improved care delivery and outcomes. For example, policy makers investing in large-scale HIE programs may seek to tender for an evaluation of such a program but have a poor/limited understanding of the research required to address such a goal. I believe a discussion providing an overview of specific approaches/studies required to address the evidence deficits would be a valuable contribution of this review. Ie to go beyond stating that " … research could better serve this effort by developing and pursuing a more deliberate research agenda designed to capture the full impact of HIE and identify the comparative role of specific factors related to …"(p ES-6 line 51)	We have expanded what we believe is the research required in the Discussion section.

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TEP Reviewer #4	Executive Summary	Having read the entire report, the description of future research on p79 provides a more specific description of the research challenges and suggestions as to how these might be tackled. I wonder whether alluding to this greater level of complexity might be useful in the executive summary.	We have expanded what we believe is the research required in the Discussion section as well as the Executive Summary.
Peer Reviewer #4	Executive Summary	P ES 6, line 41: the conclusion that "the overriding consensus that HIE should improve efficiency and quality of care is not overwhelmingly supported by the evidence." constrains the scope of the review. It may not only be premature to detect this impact but also that the study designs appear not to have been set up to differentially determine the solo impact of HIE. Thus one questions holding out such strict criteria.	We disagree that this statement constrains the scope of the review. However, we have reworded this sentence to report our overall results more precisely.
Peer Reviewer #5	Executive Summary	Page 14 (of 402) end of 2nd full paragraph.Note about systems slowing down when access increased. This might be more appropriately attributed to insufficient computer power rather than blamed on successful attraction of many users.	Noted.
Peer Reviewer #7	Executive Summary	Minor wording: On page ES-4, the phrase "usability features" is awkward and nonstandard. The authors may wish to rephrase this.	Text was changed to be less awkward.
Peer Reviewer #8	Executive Summary	ES-3 line 11 :careful here as you rightly note that the studies are often observational and these studies cannot indicate causation. You have 31 studies of HIE that report associated outcomes, not that produce outcomes.	This is a good point, and we have noted that outcomes are "associated" with HIE.
Peer Reviewer #8	Executive Summary	ES-4 line 13:put in the years please. As this study ages "the past 5 years" becomes a "moving target, ie which 5 years?	This information was added.
Peer Reviewer #8	Executive Summary	ES-4 line 40 YOu are not consistent with data being singular or plural--i don't really care but choose one and stay with it.	We corrected this to be consistent.
Peer Reviewer #8	Executive Summary	ES-4 line 57 this is not unique for HIEs--almost all of our eHealht systems show this pattern.	Noted.
Peer Reviewer #8	Executive Summary	ES-5 line 51 not your first us of IT	This has been corrected.
Public Reviewer #2	Executive Summary	ES-7 final sentence of the conclusion is repeated	This was corrected.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #1	Introduction	Page 23 Ln 24 The challenges are a little undersold. There are challenges in all research, HIE has more than is listed by the authors here (which I think do have implications to state of the evidence). For example, several evaluations of the ONC SDE program started with expectations of effectiveness designs, but failed because of implementation problems (as an example see Yeager et al J Med Syst. 2014 doi: 10.1007/s10916-014-0078-1). Kern, Ancker et al (JAMIA 2011) outlined many of the challenges of HIE/HIT research.	We now cite the Kern et al paper in the introduction and the Yeager et al paper has been included in our analysis. We have also elaborated why HIE is challenging to evaluate.
TEP Reviewer #1	Introduction	Page 24 The analytic framework is good and includes a lot of the nuances and points of context that are critical to understanding the state of literature. It would be good if these points (e.g. different types of HIE) could be incorporated into the ES. The key questions are well-defined and appropriate. In addition, the focus on harms is particularly relevant to AHRQ's interests.	We have elaborated on the research challenges in the Executive Summary comparable (but in less detail) that of the full report.
Peer Reviewer #1	Introduction	Page 2 - line 24: I disagree that "HIE is an intermediate technology". HIE is an action, the sharing information across systems, devices, or platforms. The scope of sharing health information is also broader than care delivery (i.e., public health, wellness, etc.)	We have re-written this sentence to elaborate that HIE is used intermediate to improving care delivery, allowing clinicians and others improved access to patient data to inform decisions and facilitate appropriate use of testing and treatment. As such, HIE is not specific to any health issue or diagnosis.
Peer Reviewer #1	Introduction	Line 30 - What is meant by "adoption of HIE". HIE is not a single technology like an EHR.	We have made clear that there are many forms of HIE.
Peer Reviewer #1	Introduction	I am also a little confused by Research Question 5. How is usability defined? Usability of workflow assocaited with sending, receiving, finding, and using health information? Usability of the information received? Usability of the technology platform that facilitates exchange? The authors need to strengthen the context in which HIE is described for this research question and throughout the report.	We have revised the text to be more clear how usability related to HIE is defined. We have used the authors' own definitions.
Peer Reviewer #2	Introduction	OK	Noted.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #2	Introduction	"ONC, the lead government agency for health IT development" ONC doesn't develop HIT, they coordinate federal initiatives involving HIT.	We have made clear that ONC does not develop health IT.
TEP Reviewer #3	Introduction	Well done.	Thank you.
Peer Reviewer #4	Introduction	The very-general "synthesize the literature in HIE" very quickly gives way to addressing specific questions about the clinical use and clinical consequences of HIE. While these questions are not in themselves bad, they seem quite premature given the characterization and penetration of HIE at this time. In addition, questions posed would be relevant to ask regarding any use of any information at the point of care. So it seems that the bar to which HIEs are being held is higher than even that to which we hold clinical information systems.	We disagree that mature HIE implementations cannot be evaluated now, and our call for a more detailed taxonomy going forward should allow readers of that research to discern settings like the point of care.
Peer Reveiwer #4	Introduction	The definition of health information exchange is too broad and not well-justified. There is an entry into table G that the variable "Type" which appears in the table to be free-text will eventually form the basis for better characterization of the "type" of HIE -- yet this reviewer was unable to find that characterization in the narrative. Table 1 employs the terms "Query" and "Directed" as types. On page 9, line 34, these terms are used to describe the form of the HIE, and are accompanied by the phase "consumer mediated exchange"). What remains unclear to this reviewer is whether the report treats a point-to-point between two health care providers request for information on a given patient the same as an exchange mediated by a community health data bank.	We have clarified our definition of HIE, which is aligned with the one used by ONC. Point to point exchange of information would fit the definition for directed exchange. And while we did include consumer-mediated exchange in our definition, we did not find any studies that evaluated its use.
TEP Reviewer #5	Introduction	A very clear description of the current state of the literature and its limitations regarding true outcome descriptions and evaluations.	Thank you.

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TEP Reviewer #5	Introduction	Perhaps a little more background lincluding examples) could be provided in the Introduction about the background of HIE's and a little more description about the various types of data and formats of data exchange that woudl be covered in the Evidence Report. A reader unfamiliar with the field might have a little bit of a challenging time understanding the terminology that is then subsequently used throughout the rest of the manuscript.	The report provides ample citations to HIE, so a reader unfamiliar with it can pursue the references cited.
Peer Reviewer #6	Introduction	No concerns. Well written and concise summary.	Thank you.
Peer Reviewer #8	Introduction	Good. Concise and useful. My only comment is that the intro might address how the HIE systems are labelled across countries and disciplines--see my notes of the 2 issues that could be considered overall for the report.	Our review on international studies shows there is less precision on the definition on HIE than in US-based studies, and in fact some international studies do not even use the term "HIE". So we have used the ONC definitions, which have the widest, even if not complete, consensus.
Public Reviewer #1	Introduction	Until true promulgation of CONSISTENT HIE happens across the US I think it is quite premature to study its effectivenss on anything in healthcare. What NEEDS to be studied FIRST is where and how consistent HIE is happening and not happening and why. My personal experience in SW OH is very poor and it does effect my bedside behavior in medical decisionmaking.	We agree that HIE development has been uneven and inconsistent, but the goal of this evidence report is summarize the published literature.

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Public Reviewer #2	Introduction	p.1 Last paragraph: "ONC has defined three key forms of HIE." From the perspective of Redwood MedNet (RWMN), the Office of the National Coordinator (ONC) blundered in defining the three key forms of exchange as "Directed, Query-based, or Consumermediated." 1 In their defense, these definitions were likely crafted to enable ONC to declare in response to Congressional oversight that ONC was a good steward of the HITECH appropriations. But such simplistic policy-based definitions of types of data exchange obfuscate architecturally distinct technical specifications for clinical data transport. In particular "directed" exchange conflates two different data transport architectures, therefore analysis of the literature on "directed" exchange may be misleading if the terminology ambiguity of two distinct transport architectures is not addressed. Can the AHRQ systematic review be anchored in the precise terminology of information science rather than based on nontechnical policy jargon of statute and regulation? Or will the usability of this systematic review be compromised by fuzzy and conflated data transport attributes? Failure to address this risks infusing terminology incoherence into the study design, although in AHRQ's defense absurd policy simplifications may be necessary for Congressional oversight.2 **Contextual note and full disclosure**: RWMN completed five separate HITECH subcontracts under the Statewide HIE disbursement. The five contracts were signed with three separate entities inside California. The interoperability traffic reported to ONC as required under the contracts suffered from the terminology drift and data element ambiguity noted above. The ambiguity was due to vague federal definitions for "directed, query-based, or consumer-mediated exchange." If RWMN were an article in the systematic review, RWMN would be characterized as: ‣ Location = geographic (multi-county region in Northern California covering 9,000 mi2 with a population of 1,000,000) ‣ Setting = includes inpatient, outpatient, health system, independent lab or imaging center, local HHS agency ‣ HIE type = 99.9% directed exchange, minimal query-based exchange, no consumer-mediated exchange	We agree that there are inconsistent definitions of HIE, but these are propagated in the evaluative literature and our report is a synthesis of what has been reported in that literature.

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Public Reviewer #2	Introduction	p.2 The paragraph that begins "Evaluating the effectiveness of HIE..." ends with reference number 25 but it it may actually refer to reference number 26.	This has been corrected.
TEP Reviewer #1	Methods	The inclusion and exclusion criteria are appropriate given the Key questions. The search strategy was also appropriate. Agree with the authors that a meta-analysis across the different study questions was not appropriate and a qualitative summary is the most appropriate way to proceed.	Noted. Thank you.
TEP Reviewer #1	Methods	Given the large number of returned results, I would have expected some quantified measure of screener agreement. The approach outlined is completely reasonable and appropriate, but it would be nice to know how often the 3rd reviewer was called in to settle disputes. Kappa between the two initial screeners might be low and that wouldn't necessarily be surprising or bad – given the breadth of this review (eg. Outcomes, usage, sustainability).	There are different, acceptable approaches to this task for AHRQ reports. We chose an approach that did not include calculating kappas. The text has been revised to more clearly describe our approach.
Peer Reviewer #1	Methods	The inclusion/exclusion criteria are justifiable. However, it appears some key search terms that focus on specific use cases are missing. Since exchange is an action, some studies that focus on the electronic exchange of lab test results, discharge summaries, radiology reports, public health reporting, eRx and CPOE are likely missing, since it doesn't appear that key search terms were included in the review. For example, this O'leary study may have qualified for inclusion, but I didn't see it "http://www.ncbi.nlm.nih.gov/pubmed/19267397"	We tested our search and developed and reviewed it with two specialized librarians. We found a general search focused on HIE was more efficient in capturing use cases than use case terms without the HIE terms. We always supplement searches with pearling and followup on suggestions.
Peer Reviewer #1	Methods	Additionally, I recommend searching some white papers as well. ONC has both data briefs and evaluation studies examining different types of HIE. http://dashboard.healthit.gov/evaluations/library.php The outcome measures and statistical measures are appropriate.	We did search ONC and other white papers as part of both our gray literature search and in pearling cited and recommended sources. Several have been included in the report.

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Peer Reviewer #2	Methods	This review wonders if the literature search window should have gone back to 1990. Modern HIE is a recent phenomenon. This would be akin to researching uses of the World Wide Web back to 1990, given that it was invented some years later. Frankly, I suspect articles or sources written before 2012 are probably not relevant to the topic in the present world.	While we agree that the technology has changed, we believe that some of the challenges organizations and individuals face when technology changes and strategies used to address these could be relevent. For this reason we constructed the search to include these earlier experiences. The dates the studies were published as we as when the data was collected are noted in the abstraction as this is discussed in the relevent sections of the report.
Peer Reviewer #2	Methods	It is unfortunate that search strategy ended in April, 2014. The special issue of eGEMS, Volume 2, Issue 3 (2014) Lessons from the Field: Health IT-Enabled Community-Based Transformation, arising from the Beacon communities, would have been disproportionately informatics. We all realize that studies must work with what exists at the time they are done, new research continues to be published. However, I think this special issue is especially germane.	We updated the search between the draft and final and included additional studies that were picked up during that search. We also reviewed the eGEMS articles for inclusion.
TEP Reviewer #2	Methods	: Literature Search Strategy I thought on the TEP call we also recommended CINAHL to catch allied health/nursing literature. It is listed in Figure 2 (spelled wrong), but not in any of the text descriptions.	We have revised the methods text to include CINAHL. Thank you for pointing out this error.
TEP Reviewer #3	Methods	The inclusion/exclusion criteria are well thought out, clear, and justifiable, logical. The investigators reviewed search strategies on TEP call early in project (much consideration was put into these). Search strategies are explicitly stated and detail is included in appendix. Due to heterogeneous nature of data, statistical methods not used (appropriately).	Noted. Thank you.
TEP Reviewer #3	Methods	Page 80/402: Consider changing "physician -based model" to "provider-based model"	We have made this change.
TEP Reviewer #3	Methods	Page 90/402: Typo on line 8, change not to note Page 92/402: Typo on line 26: change engage to engagement	Typo has been corrected.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Methods	Page 8 Key question 5: Usability might reflect more on the EHR product than on the HIE services. In many cases the "HIE" functionality would be hidden from the users because of the integration of the EHR with the HIE services.	We did identify studies that assessed the usability of HIE directly. We do agree that there may be other usability issues that are not address in this literature.
Peer Reviewer #3	Methods	Key question 7: The term "implementation" includes operations but to me it seems like on-going operations is important and distinct.	We did not revise the key questions for the report as they have been posted and the subject of public and reviewer comments prior to the report draft. We did clarify these concepts in the corresponding section and discussion.
Peer Reviewer #3	Methods	Key question 8: The term sustainability could be a little better defined especially since most people think of the term in regards to financial sustatinability. It is hard to tell what is included in the term which seems to include some aspects of ongoing operations.	We did not revise the key questions for the report as they have been posted and the subject of public and reviewer comments prior to the report draft. We did clarify these concepts in the corresponding section and discussion.
Peer Reviewer #3	Methods	Bottom of page 10 explains why implementation and sustainability are often lumped throughout the paper. For future research, it doesn't makes sense to lump implementation and sustainability. They are really two different things. The concept of operations seems to be lumped in sustainability or is missing.	Thank you.
Peer Reviewer #4	Methods	The inclusion and exclusion criteria are acceptable but not well justified beyond the attribution to the AHRQ guidelines. The definition of HIE is broad and not well-justified; for example, it is not clear how secure messaging would be excluded.	The text has been revised to clarify that.
Peer Reviewer #4	Methods	The review contains an adequate appraisal of the strengths and limitations of the literature base upon which the review is based. The conclusions are general and not very strong; this in part is a consequence of the literature underlying the review.	Thank you. We have revised the conclusions and while we can not strengthen the literature we have added detail to our discussion of the literature and future research needs.
Peer Reviewer #4	Methods	The review correctly characterizes some of the challenges in the HIE literature, notably determining coherent units of analysis studies conducted at varying levels of abstraction. That is, some studies examined patient arrivals at an ED, others employed broad surveys, still others examined clinician behavior. The report does little to add clarity to this situation, relying instead on attempts to integrate evidence across studies of different units of analysis.	We agree that the literature includes analyses are several levels. We found that the different levels corresponded to different key questions and we decided to include what is available in for each key question.

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Peer Reviewer #4	Methods	When appraising the quality of the studies there appears to be little attention given to the funding source and the extent of independence of the review; this was also not noted as a source of bias. It is indeed worrisome that the self-report of an institutions' self-developed HIE may be considered at the same level as an external evaluation conducted by an independent party.	We agree that funding sources may influence work, but there is no empirical evidence available to date that this is the case in this field. Given this situation we have noted this situation but focused our quality assessment on the effectiveness studies and criteria which we know directly impact bias.
Peer Reviewer #5	Methods	All OK but the criterion does not apply as well to this kind of review as to a typical clinical space.	We agree that in some cases methods developed for clinical reviews are difficult to apply to non clinical topics.
Peer Reviewer #5	Methods	Page 28 Last sentence. “Organizations are settling on a set of core services offerings”. If this set of core services is enumerated somewhere, would be interesting to see that in the report.	Thank you for this suggestion. We have added these core services to the end of this sentence - "...such as secure messaging, and exchange of information for care summaries and transitions in care".
TEP Reviewer #5	Methods	The methods emploted for this evidence report as a systematic review, seem to be appropriate for the type of literature available. Most studies were retrospective cohort analysis that analyzed only a portion of the available features and functions of an operational HIE. There was also no significant numerical or statistical evaluaion (No meta-analysis) because the nature of the studies reported to date is not congruent with agregating and analyzing the data in a standardized fashion. The authors did a good job of describing how the initial search criteria, and exclusion critera ended up producing the articles used in the systematic review. In addition, while there was not enough (or congruent enough) data for determining an initial outcome as to whether HIE is appropriate for widespre adoption and use, we were able to gain a more appropriate understanding of the state of evaluation regarding HIE's as well.	Thank you.
Peer Reviewer #6	Methods	: The inclusion and exclusion criteria appear to be justifiable.	Noted. Thank you.

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Peer Reviewer #7	Methods	Certain revisions could strengthen the methods of this report. a. Inclusion criteria and scope: There is some ambiguity about the scope of the term HIE as used in this report. The authors do not appear to have included any studies of enterprise-based HIE (such as exchanges within healthcare delivery networks), vendor-based HIE technologies (such as exchange functionality supported by the EHR vendor), services (such as ordering/delivery/access for labs and radiology), or consumer-mediated HIE (e.g., personal health records, Blue Button functions, secure messaging with providers). It is not clear whether these categories were a priori excluded from the scope of the review. We recommend clarifying the scope of the review, and if all of these categories are excluded, providing a justification of why. (See accompanying comments in results comments below.)	The text about the intervention has been revised to clarify which of these were excluded a priori.
Peer Reviewer #7	Methods	b. Phrasing of key questions: Occasionally throughout the report, the authors refer to "HIE projects" or "an HIE project" (for example, in the initial phrasing of Key Question 7). Do these refer to the establishment of a fully operational HIE organization? Or to the development of targeted services (e.g., quality improvement, results delivery, etc.) by an HIE organization? These two interpretations would have different implications for which articles should be included (see below).	We have used HIE to mean the action or process (a verb) and add project or organization or other terms when we want to refer to a noun. As HIE has been used in both senses we realize that this can be awkward. Studies included assessments of both activities and organizations at different levels of maturity.
Peer Reviewer #8	Methods	Yes, the inclusion and exclusion are explicit and sensible as well as justifiable and justified. Search strategies are good and certainly capture the HIE and exchange issues--again see my note on other names. Agree that this evidence cannot be combines (meta-analyses or syntheses). Good narrative combinations.	Noted. Thank you.
TEP Reviewer #1	Results	: Page 35 Ln 33 This is worded much better than was done in the ES (see comment above on “limitations”).	Noted and addressed in ES section.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #1	Results	Page 36 ln 9 The usage of HIE data in support of other research is a valuable feature of HIE. It is not part of any of the key questions for the review, but it would be useful to highlight this point later.	It is now addressed in the Discussion section.
TEP Reviewer #1	Results	Page 46. Summaries like Table 3 are very helpful. As with any review, the text can get a bit dense after a while so these kind of overviews are useful.	Thank you.
TEP Reviewer #1	Results	Page 48 Ln 35 Some kind of map of state counts or bar chart of (state vs national) surveys over time might be helpful in summarizing the nature of the evidence.	We tried to do this but found it unwieldy and not very informative.
TEP Reviewer #1	Results	Page 72 Ln 14 Maenpaa should be Mäenpää.	Noted. Fixed throughout.
TEP Reviewer #1	Results	Page 87 – 94 The distinction between the different levels of analysis is this section are not readily apparent to the reader. Facilitators / barriers can either be at the organizational level or the level of the individual users (the authors obviously know this). The review as structured, though, does not make any of those distinctions clear (or in the summary points). The same is true for sustainability, which really an organizational level concern. Some summary table might be useful or some summary text. The concern is about identifying were policy makers may make the biggest impact. National policy can help individual users, but funding, regulations, etc would have more impact on the organizational level adoption and investment in HIE.	An introductory paragraph has been added that clarifies this.
Peer Reviewer #1	Results	The results are appropriate. Other than potentially missing studies with the search terms, the investigators appropriately described the results in a comprehensive and cohesive fashion.	Thank you.
Peer Reviewer #2	Results	Again, within the framework of the available literature, the results reflect what is published. Nevertheless, the authors themselves point out that the “body of literature is limited in several ways…” which they enumerate in the “Implications” section of the ES (ES-6), Strength of Evidence (p75), Limitations of the Evidence Base (p78) and other places.	Noted.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #2	Results	Table 3. Put a blank line in between the rows where the subject in the first column changes (i.e. before Setting, Location, HIE type). The bold typeface does not do enough to signal a major change.	We have followed the style guide provided by AHRQ for formatting tables. We have attempted to make this table clearer.
TEP Reviewer #2	Results	"The Tripathi et al. study was unique in that researchers" Which study? no citation given.	Thank for finding this. We have added the reference number to this sentence.
TEP Reviewer #2	Results	: Results are clearly displayed by research questions. The method for display was reviewed with the TEP and is appropriate, logical. The literature flow diagram on page 34/402 is excellent (shows the number of citations for each key question). The format of key questions/key points/detailed synthesis/tabled results is clear and effective.	Thank you.
Peer Reviewer #3	Results	THe paper does a very nice job analyzing and summarizing the findings of the studies. Nice use of tables to help summarize.	Thank you.
Peer Reviewer #4	Results	The results as presented are logical and consistent with what is known about most HIT interventions: fit with workflow matters; organizational leadership support is key; governance of both the local care group and the IT organization should be aligned.	Thank you.
Peer Reviewer #4	Results	It is laudable that the report avoids both broad generalizations and specific predictions. However, this cautionary stance appears to have limited some of the value of the report overall.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	Results	The organization of the results around major questions is acceptable; however an unintended consequence is a co-mingling of findings that relate specifically to care providing facilities and findings that relate specifically to HIE organizations. One would expect that the impact of HIE on health care would be examined differently in care providing facilities from HIE organizations. For example, Table 10, which addresses facilitators to implementation and sustainability includes both those related to care providing institutions (e.g. "Reflect understand of services and work flow") as well as the HIE organization (e.g. "HIE lead by Health information Organization"). Thus, it becomes difficulty to determine whether the conclusions relate specifically to a care providing institution, an HIE provider, or some intersection of a care providing institution of a certain type and an HIE of a given configuration	Thank you for this observation. You are correct in that the different organizations may be responsible for HIE than for delivering care. However, in some cases it is the same organization and when the responsible organization does not provide care, implementation and sustainability need to incorporate the perspective of both types of organizations.
Peer Reviewer #5	Results	Very good detail presented in the results section. Yes, the characteristics of the studies are clearly described. Figures, tables and appendices are excellent. For their quantitative analysis, their exclusions were right. To get a better sense about how the systems worked for classification purposes, some descriptive studies would have been useful. But the distinctions between the different kinds of HIEs and what they accepted as an HIE is not as clear as it could be. Needs an expanded section and examples of the distinction and even better (but probably not possible) would be to characterize their results based on the type and maturity of the HIE.	We have changed text and tables to discuss types when the authors provided that level of detail.
Peer Reviewer #5	Results	Page 50 middle of 2nd full paragraph. “Physicians reported being able to both send and receive data.” Not clear what they mean. What kind of data, for what purpose, to whom? Are they doing it? Is this a potential or real? Is someplace really doing this?	The details about what was sent and received appears in the Results cell of Table 4 - the Patel study, reference #80. In the interest of brevity, we did not include this same detail in the second paragraph.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Results	Page 61. The discussion regarding less use of HIE by small practices and larger systems could use further discussion. Accept that it is true. But, the discussion mixes communication between parts of a large system (e.g. VA), with communication developed among independent organizations. So that confounds the discussion. If we are talking only about independent organizations, connecting an HIE to a large independent system, per unit of data obtained, is cheaper than connecting to many small practices for the same amount of data. So connecting with large systems even if they are independent could be expected to be better. [And am not sure I would classify links between different places within a single large organization as an HIE. But if they are, the studies from single organization "HIEs" should be segregated/distinguished from those from traditional HIEs developed from independent organizations	The reviewer makes a valid point that communications will differ, depending on whether organizations are or are not independent. We purposefully separated the discussion of the VA system from the discussion of statewide initiatives in small practices. The discussion of the VA system centers around matching patients between the VA and external organizations. The discussion of small independent practices is the focus of page 61. We also agree with the reviewer that we did not consider as HIE, links between different places within a single large organization.
Peer Reviewer #5	Results	Page 77 Line 10-22. Again, the definition of types is unclear: (direct vs. query based, and centralized vs. decentralized). Direct is the name of a technical mechanism developed by ONC using an email-like understructure-- it is often discussed along with the other ONC method (CONNECT) -- is that what you mean? Are you are assuming it is "push"? If so, say so. Are you thinking of query based as "pull"? The two can get tangled so an email (DIRECT) system could send a query to ask for data (pull) and then the queried system would send the response via email (push), or the source system could spontaneously send an email with new data it produced to a single provider . But that could only be useful when the provider and source institution have some prior connection and would not think of that as an HIE. All HIEs permit or use queries, whether initiated by a computer at check in at the patient care site or by the provider caring for the patient.	Thank you. We have added a section in the introduction to clarify the types we are including, based on the ONC (query-based or pull vs. direct or push). We gave also edited this section to clarify what type means. Type for this report was based on function and not architecture. We provide details on architecture when the authors provided them in a table but do not discuss architecture as the authors did not consistently provide this level of detail or used different descriptions to present the architecture.

Commentator & Affiliation	Section	Comment	Response
		The federated ones may be of two types. One that queries directly to the source EMR and another that pre-sends all (or a subset) of its local EMR content to what is called an Edge server, also local to the source site. The big advantage of the centralized system – of which 1) Regenstrief, 2) Memphis, 3) CRISP (https://crisphealth.org/ABOUT/General-Info, a very successful HIE in Maryland per a medical resident in Baltimore who is with me for this month), and 4) the insurance plan based in Mass are examples – is that centralized systems receive data from the source system more or less as it is produced and (usually) via HL7 v2 messages. The central system can process, check, and fix (when needed) the data, and link patients ahead of time, so that things are looking "good" by the time the provider logs in. The centralized system also yields retrieval efficiencies and is not affected by the down time or slowness from one or more of the decentralized systems. The other advantage of centralized is that the organization can develop expertise and special programs to detect and fix errors. Our original plan in Indiana, proposed explicitly in our grant application, was to have separate servers at each of the participating hospitals (edge servers). But it was impossible to get enough attention even to get computers installed, much less the more complicated processes for mapping terms, reviewing, and providing feedback on bad HL7 messages or bad content. The other hospitals were happy for us to take it over; so we hired people who concentrated on, and could become "expert" at those matters. A subtle issue: both Regenstrief and Memphis did put data from each source in a separate segment of their centralized medical record database, but these were not Edge servers as in a federated system. And the segmentation should not be overemphasized. You can segment data easily in modern databases but have them behave as one unified database.	

Commentator & Affiliation	Section	Comment	Response
		The more restrictive the consent policies, the less use the HIE will get, and organizations can easily crank down the access door so tightly that providers will almost never use the system. But think Memphis and RI were very close in design and would call them both centralized databases. Segmenting was just a way to give the participants options for control and make it easy for them to withdraw from the collaborative. There are still other layers of difference. In the ERs, providers did not have to remember to query the HIE or spend time doing so. The check in system sent a message to the central HIE, and the HIE generated a compact report summarizing key patient data. That report was put on top of the encounter papers. Providers could see it without effort. In other settings, providers did log in and initiate access to the Indiana HIE themselves. So think you should drop the “query based” as a distinction and find other classifiers, such as Centralized/decentralized (and decentralized with edge server versus not), etc.	

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Results	Page 77 Line 24-27. As noted before, what you are referring to by "directed" or alert is not at all clear. These issues might be tangled with the inclusion of systems that were independent and systems that were naturally linked under one authority, such as the VA. Was the alert describing a process in the VA sending alerts about patients who visit a second VA hospital? It would be ideal if you could separate discussion of HIEs made up of independent institutions from those linked under a central authority (as is the case for the VA hospitals and Kaiser). The latter have the advantage of a single hospital number and provider authentication, which solves many problems and may be closer to integrated care systems than an HIE. What does it mean to say that the providers received cCDA documents? Does that really mean that cCDA content was delivered to their EMR? Did they have to look for them in their own EMR, or did they get them in their email inbox? The former still implies the provider having to take an initiative and "querying". To my understanding, the latter will only work if the sender of the cCDA knew the provider. I would not think it would work for ER providers.	Thank you. These details have been added to the summary table at the end of this section when the authors provided them. The section in the text was deleted as we felt the level of detail wasn't sufficient to make comments.
Peer Reviewer #5	Results	Page 77 Line 27. Have brought this up before. Need clarification of how the DIRECT and directed linkage works with much more detail so the reader could understand how they fit compared to a classic HIE. Shipping information by email is probably the DIRECT connect mechanism. The document was not clear what stimulated these deliveries. And how did the sender know when and to whom to send the content?	Thank you. These details have been added to the summary table at the end of this section when the authors provided them.
Peer Reviewer #5	Results	Page 77 Line 31. These alerts about admissions etc. are parallel to what has long happened by post office mail. These are sent to whomever the patients say is their doctor. (I still see them sent to me by postal mail by mistake.) This is not an alert in the sense that there is smart logic behind it, and I would not have thought this would require an HIE to do. So again, clear definitions among the kinds of HIEs you examine would help	Thank you. These details have been added to the summary table at the end of this section when the authors provided them.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Results	Page 77 Line 33. Was the logon directly into the home-based community service system, and were all of the providers who could already assigned password and access privileges? If so, not sure I would consider this an HIE. Providers who staff at multiple hospitals will have access privileges at all of those hospitals, whether or not an HIE has been established. So again, there is a spectrum of HIE-ness and worry that the lack of distinction will end up obscuring the conclusions. To avoid confusion about what is an HIE, might at least want to, under separate sections, report about those that require providers to be pre-assigned password access and offer minuscule integration of anything-- from the more typical HIE-ish systems.	The articles often don't provide this level of detail. Each was read carefully to confirm that HIE occurred and the details were put in the summary table.
Peer Reviewer #5	Results	Page 77 Line 38-40. Again, not clear what is pull and push and how they operate – and how they related to class of query-based system. One study describes the ability to include a "copy to" (CC) in the order. That "copy to" feature is and has been a "standard" function on many systems even in paper-based systems' orders. Does that make the system an HIE?	The Campion article was re-abstracted to clarify this section. Details were added to this section.
Peer Reviewer #5	Results	Page 77 Line 41-42. Being able to pull any result from any order is more credible as an HIE function. But with no further information, hard to picture how this could work. How would an independent provider know when to look for the results of an order? Does it depend on a central server to hold all of the results? Were results organized by patient in a central system? If the latter, this would be a full-fledged HIE. However, the reader couldn't know without a bit more detail.	The Campion article was re-abstracted to clarify this section. Details were added to this section.
Peer Reviewer #5	Results	Page 77 Line 42-45. Not surprising that push was preferred over pull -- because it avoids the log in and other problems of logging into and navigating through a "foreign system	Agreed.
Peer Reviewer #5	Results	Page 78 and 79 Table 8 Workflow clearly makes a difference, but I think the phrase workflow obscures a simpler reality that really boils down to the provider time cost of obtaining the information. Bad workflow can add to time cost, but is not the only contributor to the time cost of using an HIE. The more effort (time cost) required of the provider, the less the system will be used. You have documented that providers prefer to use HIEs when they don't have to spend time getting the data –as	We agree with your changes to relabel the barriers and facilitators. This section was re-organized to have main barrier themes of: Lack of critical mass; Inefficient workflow; Poorly defined interface.

Commentator & Affiliation	Section	Comment	Response
		occurs when staff does the work of pulling records, or when the data is pushed to them (though, it is not clear how the remote system knows when to push to a care site unless the check-in process triggers a request.) Or do the care sites request some chunk of data and present the provider with a printed document?2 (That is the way the EDs did it in Indiana,2 and the way we (and others) pull medication data from SureScripts.1 It is a foregone conclusion that time constrained providers could hardly ever invest 2-3 minutes trying to get patient data from an HIE or outside source. The difference between usage rates when time costs per access are high versus low is striking. RxHub (who later threw in with Surescripts) provided medication profiles to a hospital ED in Indianapolis and to another ED at a Boston Hospital. At the Indianapolis hospital, with opt out permission, the hospital registration computer sent an HL7 request to RxHub, which responded with a medication profile , the hospital computer printed out any profiles that RxHub returned, and nursing staff placed them with the other encounter documents that physicians reviewed before seeing the patient. No provider effort. In Boston nothing was done at check in time. If providers wanted to review RxHub medication data, they had to log in with the patient at their side and the patient had to verify their permission then and there. HUGE PROVIDER EFFORT. (I believe that process has since been eliminated in Boston.) The Indianapolis hospital's ED has about 275 patients per day, of whom requests were made for all but about 3%, and about 30% of the requests had RxHub medication profiles. So, the provider saw profiles for about 90 patients per day (or 630 per week). I think the Boston hospital had a similar ED volume. RxHub (not published) reports and back then they got only 4-6 requests PER WEEK from the Boston hospital. No surprise. The first category of barriers might better be described as the need for a critical mass of patient data not otherwise available in the home system. This could then subsume two	

Commentator & Affiliation	Section	Comment	Response
		of the points in the third bullet. And that bullet could focus on access interface and data presentation.	
Peer Reviewer #5	Results	Page 82Line 11-12. The HIE delivers data for patient care, HIPAA does not put different constraints on the use of textual data versus lab data for patient care. So don't understand the statement that textual data was excluded "for confidentiality reasons." Seems like they shot themselves in the foot by not including radiology reports and hospital discharge summaries.	We agree but reported exactly what was found in Rudin 2011, p.54. It may mean textual notes of a sensitive nature but we didn't want to interpret.
Peer Reviewer #5	Results	Page 82Line 15. Paper report faster to read. (This could also be due to the fact that someone else might have pulled the paper report, so no time investment to log in and find the patient. Or that paper reports are intrinsically easier to view because of their higher resolution and larger size. Could you clarify whether the places that liked paper had the reports produced by staff?)	These papers did discuss proxy users but the theme of the result was the need for a short concise report so that the physician doesn't have to click through pages of details that aren't helpful at the time of care.
Peer Reviewer #5	Results	Page 82Line 23. The slower with more users suggest the system had under-powered computers.	Agreed.
Peer Reviewer #5	Results	Page 82Line 26 -27. Interesting	Noted.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Results	Page 82Line28-29. Integration has many shades of gray. Having single password to get to the local system or the HIE is important, because it saves time and the user will not forget the password he/she uses every day but will forget the password of a separate HIE not used frequently. But single sign-ons can be implemented on top of individual systems with otherwise separate sign-ons. Any sense of which of the systems had single sign-ons across institutions? The advantage of integrating the data is that it leverages users' navigation knowledge of their home system and if that implies integration of data (a hemoglobin from many sources shows in one line of a flowsheet) that is another huge advantage. But single sign on and data integration can be providedwithout integrating into the home system. For the Indianapolis hospital, the HIE was the integrator and still is. Just some thoughts.	These paper were reviewed again and notes about integration were added to the summary table at the end of the section. Most studies didn't provide this level of detail.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Results	Page 90 Line 33-34. Would be helpful to go beyond saying standards were needed, and adding what they were needed for. Here are some potential reasons. One cannot put data from multiple organizations onto a single timeline/flowsheet unless they all use the same test, and report, identifiers -- whether it is a diastolic blood pressure or a chest X-ray. And it is much harder to provide a common organization – e.g. chemistry test, then hematology-- or to alphabetize radiology reports if the results from different sites do not have the same (or standard) names. This is a VERY important point that is usually glossed over. LOINC provides a universal identifier that is increasingly available from referral labs, instrument vendors, cCDAs, and is increasingly required to be supported natively within EMRs (see MU3 proposed regulation).4 As standard codes accompany data from source systems, integration of clinical data within HIEs will be much easier and cheaper and HIEs will be able to prosper. Considerably more investment is require by an HIE to standardize identifiers of reports and observations, but without it, data from many sources cannot be properly integrated. As MU pushes requirements about coding tests and vital signs and other things, it will become easier.	We believe that specifying standards to this level of granularity goes beyond the scope of this report.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #5	Results	The detail in the results section were complete and appropriate for this systematic review. The initial 8 questions (and their subquestions) were collapsed during this seciton into approximatey 5 ultimate sections due to overlap in topics and to limited studies done in certain areas. The grouping of studies and key desctiptions seemed logical and appropriate given the articles available. The tables are well organized and easy to use for the ppruposes of understanding the "direction" and "strength" of a studies outcome. The study itself is somewhat focused and could use a few more examples to more readily help the end users understand how different HIE's actually (and in theory) would potentially impact the outcomes of interest.	Thank you.
Peer Reviewer #6	Results	In general, the results are well written and organized.	Thank you.
Peer Reviewer #6	Results	Page 60 line 26, perhaps clarify the concern about how slowly hie updated. The reader may not recognized that this concern is about data exchange, as opposed to software or hardware upgrades.	Thank you. We went back to the original source and the emphasis was that the exchanged information was not real time not that the software or hardware needed updates. We have now clarified the text.
Peer Reviewer #6	Results	Comments about cost benefit may be biased toward the null unnecessarily. Authors site limited sites of study as reason for low confidence. Seems unfounded.	We do not discuss cost benefit in our report.
Peer Reviewer #7	Results	Overall the results section is strong. However, there are potentially missing articles, depending on the precise definition of the inclusion/exclusion criteria (see comments above in the methods section). a. Services: If the authors intend to include electronic exchange of patient-level data including access to prior laboratory results and radiology reports (as discussed above in the methods), then a key article that should be included is McCormick et al, Health Affairs 2012, which measured the effect of electronic access to prior lab and radiology results (Note that McCormick and colleagues did not clearly distinguish between across-institution [HIE-type access] and within-institution access, so depending upon the AHRQ authors' inclusion criteria, this article might be eligible for inclusion).	As the reviewer notes, the McCormick paper did not distinguish whether test results came from a local EHR or an HIE system, and therefore did not meet our inclusion criteria for definition of HIE.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #7	Results	b. Consumer-mediated HIE: Similarly, if the authors intend to cover consumer-mediated HIE, then key omissions include: multiple recent surveys about consumer adoption of PHRs and consumer-mediated HIE conducted by academic authors and respected research organizations such as the Pew and the California Healthcare Foundation; as well as the growing body of work about effects of PHR-delivered interventions on medication reconciliation (Schnipper 2009), diabetes processes and outcomes (U Sarkar etc.), hypertension outcomes (Wagner 2012), etc.	These important PHR studies did not meet our criteria for HIE.
Peer Reviewer #7	Results	c. HIE projects vs. HIE: As described above, the key questions are ambiguous about whether the focus of the report is intended to be on the establishment of a fully operational HIE on the implementation of specific services offered by HIE organizations. If the latter, a variety of other articles should be considered for inclusion in this report. One example would be Ancker et al JAMIA 2014, on the barriers to implementation of an HIE project to give patients access to their HIE data.	We excluded this study because we only assessed studies of implemented HIE.
Peer Reviewer #8	Results	: Good narrative combinations that are well described and summarized. Tables are good--very standard and clear. I did not see studies that were left out but I am not an expert in the field. I also did not see any studies that were included that should have been left out. Nice grading of the quality of the studies--and notation that many could not be evaluated	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #8	Results	I have very few comments and feel that some of them are rather minor, and could be related more to copy editing sorts of things that a lot of substance. Two issues I would like to see in the report in some manner are as follow. I would like the authors to consider them but not necessarily change their document. Both deal with some of the issues that are common across most of our eHealth/informatics tools and our base of research evidence. I too have "done" an AHRQ report (Medication Management and Health Information Technology). One of the biggest issues we ran into was with our searching. Many informaticians, especially across countries and discipline areas use different terms for the same thing, (e.g., EHR, EMR and ePrescribing/Order entry for medications). The search was comprehensive and checked. It seemed to rely heavily on the presence of the terms "exchang:" and HIE. I would like to see something about this lack of standardization of terms as one of the challenges in this project. In Canada we are doing some HIE work but do not use the term to describe our work.	We address the need for standardization of terminology in the Discussion section concerning taxonomy.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #8	Results	Second, another of the major challenges to research and evaluation in our field is that often the same people who develop and integrate our tools are the same person or group that does the evaluation. This dual responsibility (development and evaluation) could be seen as a potential conflict of interest or at least a challenge to objectivity. Is this something the authors might like to comment upon in their assessment of evaluations being so often positive? An article that describes this phenomena of who does the evaluation is talked about in some of the work by Haynes and his work on evaluation of clinical decision support systems as for example, Roshanov PS, Fernandes N, Wilczynski JM, Hemens BJ, You JJ, Handler SM, Nieuwlaat R, Souza NM, Beyene J, Van Spall HG, Garg AX, Haynes RB. Features of effective computerised clinical decision support systems: meta-regression of 162 randomised trials. BMJ. 2013 Feb 14;346:f657. doi: 10.1136/bmj.f657. PubMed PMID: 23412440. From the abstract: “Finally, most systems were evaluated by their own developers and such evaluations were more likely to show benefit than those conducted by a third party.” Again, good work and I look forward to seeing this released.	We agree, and now cite this paper in the Discussion section.
Peer Reviewer #8	Results	Literature flow diagram: spelling should be "PsycInfo" and "CINAHL"	Noted. This has been fixed.
Peer Reviewer #8	Results	Table 1, page 15, line 24: Reporting rather than testing?	We have replaced all instances of ordering and test ordering with testing, which we believe is the better word.
Peer Reviewer #8	Results	Page 20, line 43: what is this? per oderer, per patient, per hospital? total costs?	The studies did not specify the details on lab test ordering, other than to provide an aggregate measure.
Peer Reviewer #8	Results	Page 21, line 20:for the whole system? one hospital? what percentage of costs is this?	The studies did not specify the details on lab test ordering, other than to provide an aggregate measure.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #8	Results	Page 21, line 51: over what period of time?	We now note this was over 16 months
Peer Reviewer #8	Results	Page 22 line 25: Public health is very different across countries. Please add country of these studies.	The table notes these are all US studies but we have added this in the text.
Peer Reviewer #8	Results	Page 22 line 47: Adherence of what? people taking medicines, clinicians and guidelines?	We now note this was patient adherence to taking medications prescribed based on evidence-based guidelines
Peer Reviewer #8	Results	page 23 line 22: to pateints and families?	We now note this is to primary care physicians
Peer Reviewer #8	Results	page 23 line 25: to who?	We now state this is pharmacy information provided to physicians in the ED
Peer Reviewer #8	Results	page 23 line 34: what is it?	It is satisfaction, and this sentence reads clear to us
Peer Reviewer #8	Results	page 23 line35: for who?	For patients, and the sentence reads clear to us
Peer Reviewer #8	Results	Page 24: add PCP to abbreviations list	This was added.
Peer Reviewer #8	Results	Page 28 line 30: picky but can an HIE complete a survey?	This was corrected.
Peer Reviewer #8	Results	Page 29 line 12: out in the year as this will not stad the "test of time"	This was revised.
Peer Reviewer #8	Results	Page 29 line 25: should read "Centers for Disease Control and Prevention"	This was corrected.
Peer Reviewer #8	Results	Page 41 - Table 6: This column has a different order than the other tables--state first and then city.	This was corrected.
Peer Reviewer #8	Results	Page 53 line 9 :official name is The Netherlands	This was corrected.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #8	Results	Page 68 line 15: were?	This is a direct quote and was not altered.
Peer Reviewer #8	Results	Page 69 line 9: not clear what NOT is	This word was removed.
Peer Reviewer #8	Results	Page 69 line 34: studies?	This was corrected.
Peer Reviewer #8	Results	Page 70 line 19: not clear	This sentence was revised to more clear.
Peer Reviewer #8	Results	Page 71 line 26: engagement?	This was corrected.
Public Reviewer #2	Results	p.27 “Level of Use ... by Type of HIE” is also a good location to comment on the issue of ambiguity in the HIE classification types promulgated by ONC.	We describe the classifications given by ONC, but do not provide a critique of this information, as this was out of the scope of the project.
TEP Reviewer #1	Discussion	Page 95 Ln 8 This statement has occurred repeatedly in the review. If clinical is solely “disease occurrence” or death then it is accurate. However, there are two studies that in my mind seem very clinical and have to do with the avoidance of harm: Bailey, J. E., R. A. Pope, E. C. Elliott, J. Y. Wan, T. M. Waters, and M. E. Frisse. 2013. “Health Information Exchange Reduces Repeated Diagnostic Imaging for Back Pain.” Ann Emerg Med. Bailey, J. E., J. Y. Wan, L. M. Mabry, S. H. Landy, R. A. Pope, T. M. Waters, and M. E. Frisse. 2012. “Does Health Information Exchange Reduce Unnecessary Neuroimaging and Improve Quality of Headache Care in the Emergency Department?” J Gen Intern Med.	Key Question 2 actually asks whether harm results from HIE, and we found no studies that addressed this question. We do include these two studies by Bailey et al. in the report with regards to intermediate clinical outcomes.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #1	Discussion	Page 97 This is always an element of "paper chasing" with reviews, but another review was also concurrent with this one. Despite The Spread Of Health Information Exchange, There Is Little Evidence Of Its Impact On Cost, Use, And Quality Of Care. Health Aff March 2015 34:477-483; doi:10.1377/hlthaff.2014.0729	We now cite this paper in the introduction. We also reviewed all its references and added some of the studies it cited into our analysis.
TEP Reviewer #1	Discussion	Page 98 Ln 28 The "health IT leader" concern is really important as the rest of this section. However, these ideas are called out in the ES or the abstract. A concern is that a "high level only" reader who doesn't progress past those sections will never see these ideas. And they are really important to the context of the findings.	We have updated the ES to be more consistent with the Discussion section.
TEP Reviewer #1	Discussion	Page 99 Ln 49 This is an important point, we don't know about substitution effects (either for good or bad).	Thank you.
TEP Reviewer #1	Discussion	Page 100 Ln 8 These recommendations are fine, but big ones are missing: money and time. This goes back to the challenges of doing HIE research earlier. If there is to be a stronger evidence base, there has to be sufficient investment (both government and private) to get it. There also has to be a reasonable expectation from funders and implementers about the time it will take to get to any type of impact on outcomes. For example, all the SDE grantees wanted to change outcome in utilization, but their grant and evaluation funding ran out long before many of them got mature enough to even start to look at those things.	As the reviewer knows, money and time running out for evaluation after a health IT grant proposal is very common. We have added a last paragraph to the Discussion driving home this point.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #1	Discussion	As written all the the recommendations are really at evaluators / researchers. The call to better measurement, the call to better designs, broader frameworks, etc are all research decisions and probably things most researchers know or want to do. Everybody would love to do an RCT, but have to choose the approach that best fits the context. The authors could make recommendations to approve the context of the research. The researcher is only one piece of the puzzle: the HIE organization, the IT vendor, the funders, the users, the implementation sites, etc. To focus all the recommendations on researchers only misses a lot of areas that can be improved and are often outside the researcher/evaluator's control.	We agree, and have broadened our call for evaluation by all stakeholders.
TEP Reviewer #1	Discussion	Page 100 Ln 17 “have,positive effects” is missing a space.	Space was added.
TEP Reviewer #1	Discussion	Page 101 LN 5 “Inadequately” seems like a judgment on the quality of research. If the research isn’t there, it be might be better described as “insufficient”.	We agree, and have made this change.
TEP Reviewer #1	Discussion	Page 100 Ln 10 The barriers in the conclusion are all individual, where are the organizational barriers (which if no organizational adoption no potential for individual adoption).	We do not read our statement as excluding organizational issues.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Discussion	I have some qualms with the Discussion. I strongly agree that HIE needs to be more thoroughly examined, but I don't think authors appreciate the complexity involved with examining HIE effects on key clinical outcomes. Realistically, the literature base is not likely to show clinical and economic impacts. Once providers have interoperable EHRs they are not going to withhold sharing patient information to participate in a RCT. HIOs are trying to demonstrate value to users, so they are also not going to withhold key clinical information for a study. HIE also does not occur in a vacuum. There are countless confounding factors effecting outcomes. So how do we shift the research paradigm to start asking different questions? Examining exchange is going to become more complex as open-APIs become ubiquitous, and exchange is not necessarily an action, but is facilitated through applications and other platforms. I strongly encourage the investigators to augment the discussion, and comprehensively examine challenges with evaluating HIE.	We agree, and have added more details about how prospective evaluation may be done in the future.
Peer Reviewer #2	Discussion	The authors' admonition that future work on "how" HIE should be implemented rather than on "whether" it should be, is correct in the opinion of this reviewer. However, this review does not share the view that this should be done in the context of a socio-technical hierarchy, but rather should examine whether new HIT exchange technology, such as the RESTful FHIR mechanism, may be a more scalable, affordable, and sustainable framework and thus supplant the present awkward infrastructures around CCD/cCDA generation.	We agree, and have elaborated our call for a taxonomy that includes such technical details.
TEP Reviewer #2	Discussion	The authors have presented a clear summary of the currently available, though limited, research. While reading the report I thought of several important ideas for follow-up studies based on limitations and gaps they discussed.	Noted. We reviewed all paper suggestions.
TEP Reviewer #3	Discussion	Discussion/conclusion clearly stated with key finding bulleted and then linked to what is already known.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Discussion	Pages ES-6, 69, 71 and table on page 73: This comment is not so much targeted at this report, which is a summary of reports, but towards future studies. The health care industry needs to have a more nuanced discussion when discussing/researching standards for HIE. There are actually a lot of standards so when people talk of a lack of standards what do they really mean? is it gaps among the standards, too many standards to choose from, standards that are not constrained enough, or standards that don't meet needs? Discussions are usually too general to be helpful in trying to advance that area forward.	Our call for a more detailed taxonomy should address these concerns.
Peer Reviewer #3	Discussion	Findings were fair and balanced. The paper did not try to overreach. Recognized the applicability of the findings and the liitations of the evidence.	Thank you.
Peer Reviewer #4	Discussion	The document appears to incorporate the correct literature related to HIE and use of HIE in institutions, and does not appear to overlook any important literatures. Limitations of the study are well-identified.	Thank you.
Peer Reviewer #4	Discussion	The findings are presented as straightforward restatements of the results,and the conclusions flow in a logical manner. However this reviewer would have been pleased to see better application of theories of change, human cognition or human computer interaction, innovation adoption, systems life-cycle or some other framework to provide richenss and insight based on all of the data that were collected. There is too little speculation or insight offered in the answering of the questions. Plans for future research seem to be guided more by gaps found in the existing literature rather than by any compelling reasons to fill those gaps.	Application of theoretical frameworks is beyond the scope of this report, but we acknowledge that it should be address in future research.
Peer Reviewer #4	Discussion	A clear conclusion is stated: HIE can reduce utilization of health services in an ED (eg. laboratory and imaging studies). The link between this finding and outcomes of care is not evidence in the literature and there is no evidence of the economic impact of HIE. It is likely that these findings will be disappointing to proponents of HIE.	Thank you.

Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #5	Discussion	The outcomes from this systematic review (Like many) are amibivilant about the specific recommendations regarding HIE adoption, implementation or support that an organization, region or state can or should undertake to foster HIE. The potential reasons and rational for this are well explained by the authors and are approptiate given the limited number of articles focused on evaluating outcomes of HIE. The study limitations were appropriate and seemed well informed	Thank you.
Peer Reviewer #6	Discussion	The authors have done a commendable job of summarizing the literature. One weakness in this discussion is that the overall trends in each area are not as well outlined. Some attention is given to the research agenda, but there could have been more. For example, there seem to be specific gaps in the literature, such as pediatrics, healthcare disparities, and patient centered outcomes. This did not appear to get significant coverage in the discussion.	We agree, and have added advocacy for addressing these issues in future research.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #7	Discussion	The authors are justified in their conclusion that research on the effects of HIE is limited, and that the majority of existing research relies on weaker approaches such as retrospective methods or survey methods. They appropriately call for additional research with more comprehensive scope, more rigorous study designs, and more thoughtful coordination between research approaches. We would recommend, however, that the report give more salience to the central reason why much of the research to date has been limited in scope, which is the extremely limited adoption of HIE nationwide. Without much higher rates of adoption, sample sizes and degree of exposure to the intervention will both continue to be far too limited to expect studies to be able to detect meaningful quality, safety, or cost effects. We recommend that the conclusions of this report better explain the need for continued studies of development, implementation, and use (in which qualitative and mixed methods are likely to continue to be valuable), while acknowledging that levels of use must continue to rise before classic health services research approaches such as comparative effectiveness studies or outcomes studies can be applied broadly.	While we agree that more mature implementation of HIE nationally would provide more robust evidence, there are sufficiently mature HIE implementations to allow conclusions about HIE to be reached.
Peer Reviewer #8	Discussion	Section was good. See my notes on the two issues that might be listed as challenges: searching using other terms and also the fact that often in eHealth/informatics the people who develop the tools are those that evaluate them and this often leads to potentially "rosy" conclusions. I have included a reference supporting my statement.	We have added a recommendation that evaluation be done by researchers external to the HIE implementation.
Public Reviewer #2	Discussion	Excellent. Well done.	Thank you.
No comments received.	Conclusion		
No comments received.	Figures		

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer # 3	References	Some literature that might be considered (they weren't listed in the report and don't know whether they were considered already): QUERY-BASED EXCHANGE: KEY FACTORS INFLUENCING SUCCESS AND FAILURE, Genevieve Morris, Scott Afzal, etc. September 30, 2012 HIE DRIVEN SUBSCRIPTION AND NOTIFICATION SERVICES: MARKET ASSESSMENT AND POLICY CONSIDERATIONS, Genevieve Morris, Scott Afzal, etc. September 13, 2012 CONSUMER ENGAGEMENT IN HEALTH INFORMATION EXCHANGE, Genevieve Morris, Scott Afzal, etc. September 30, 2012 HEALTH INFORMATION EXCHANGE SERVICES IN SUPPORT OF DISASTER PREPAREDNESS AND EMERGENCY MEDICAL RESPONSE, Genevieve Morris, Scott Afzal, etc. April 21, 2014 Addnitionally, the following studies by NORC for ONC, might be considered if not already, located at http://www.healthit.gov/policy-researchers-implementers/reports#state-hie-reports Case Study Report: The State HIE Program Four Years Later: Key Findings on Grantees' Experiences from a Six-State Review [PDF - 835 KB] - December 2014 Key Challenges to Enabling Health Information Exchange and How States Can Help [PDF – 442 kb] – August 2014 State Approaches to Enabling HIE: Typology Brief [PDF – 4 MB] – August 2014 Case Study Synthesis [PDF - 875 KB] - February 2013 Case Study Report: Health Information Exchange (HIE) in Maine [PDF - 375 KB] - November 2012 Case Study Report: Experiences from Nebraska in Enabling Health Information Exchange (HIE) [PDF - 400 KB] - November 2012 Case Study Report: Experiences from Texas in Enabling Health Information Exchange (HIE) [PDF - 350 KB] -	We reviewed all suggested citations using our inclusion and exclusion criteria.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	References	Fung KW, Kayaalp M, Callaghan F, McDonald CJ. Comparison of electronic pharmacy prescription records with manually collected medication histories in an emergency department. Ann Emerg Med [Internet] 2013 [cited 2014 Jun 17];62:205–11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23688770	This is not a study of HIE but rather is of medication data collection.
Peer Reviewer #5	References	Simonaitis L, Belsito A, Warvel J, Hui S, McDonald CJ. Extensible Stylesheet Language Formatting Objects (XSL-FO): a tool to transform patient data into attractive clinical reports. AMIA Annu Symp Proc. 2006:719-23	This is a technical study and does not provide evidence to inform any of our key questions
Peer Reviewer #5	References	Grannis S, Overhage JM, McDonald CJ. Real world performance of approximate string comparators for use in patient matching. Stud Health Technol Inform. 2004;107(Pt 1):43-7	This is a technical study and does not provide evidence to inform any of our key questions
Peer Reviewer #5	References	https://www.federalregister.gov/articles/2015/03/30/2015-06685/medicare-and-medicaid-programs-electronic- health-record-incentive-program-stage-3	This is a technical study and does not provide evidence to inform any of our key questions
Peer Reviewer #5	References	Adler-Milstein J, Bates DW, Jha AK. A survey of Health Information Exchange Organizations in the United States: Implications for Meaningful Use. Ann Intern Med. 2011;154:666-671.	We cited this study (reference 78).
Public Reviewer #2	References	http://www.healthit.gov/providers-professionals/health-information-1 exchange/what-hie	We cite the ONC definition of HIE in the report.
Public Reviewer #2	References	https://www.youtube.com/watch?v=I1wg1DNHbNU	This is a music video for "Once in a lifetime" by Talking Heads and is not relevant.
No comments received.	Appendix		
TEP Reviewer #1	General	Clarity and Usability: The report is well structured. A couple of additional summary tables/figures (as noted in review) would be helpful to summarize the findings. The implications will be clearer if the authors can link their recommendations to	We believe that the tables as we have them present a complete overview of the findings.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	General	Overall, this report is incredibly thorough and meaningful. One key issue I have with the report is HIE verb/noun confusion. It is stated early on that the authors are defining HIE as the "sharing of information across boundaries of health care organizations." However, throughout the report, HIE is used as a noun. Here are some examples "use of HIE" rather than "HIE use". Or on ES-3 line 31 "than an HIE".	We have clarified from the beginning, and made updates to the text, that we view HIE as a verb or activity-based noun, and that HIE implementations and organizations are described as such.
Peer Reviewer #1	General	I also find the term "use of HIE" confusing, as I interpret it as "use of sharing health information." Additionally, it may aide the reader when referring to entities facilitating exchange, such as RHIOs, to not use the term "HIEs". I encourage the authors to consistently use the term HIE.	As noted in the previous line, we have made our use of terminology more consistent.
Peer Reviewer #1	General	The report is well structured and organized.	Thank you.
Peer Reviewer #1	General	To inform policy-makers and practice desicions - please see my comment on the discussion and conclusion. A comprehensive discussion on the complexity of studying exchange and helping to guide a paradigm shift in how exchange is studied and the value is understood would be incredibly useful.	The Discussion has been elaborated to include this issue.
Peer Reviewer #2	General	The overall report, while limited by the source literature, appears to be an accurate characterization of published reports available at the time of completion. Faint praise perhaps, but that reflects more on the state of the literature than the report.	Noted. Thank you.
Peer Reviewer #2	General	Application to policy will be limited, though not as a consequence of structure or erudition, but rather the paucity of the literature.	Noted.
TEP Reviewer #2	General	Overall, this report is well done, well written, and well organized.	Thank you.

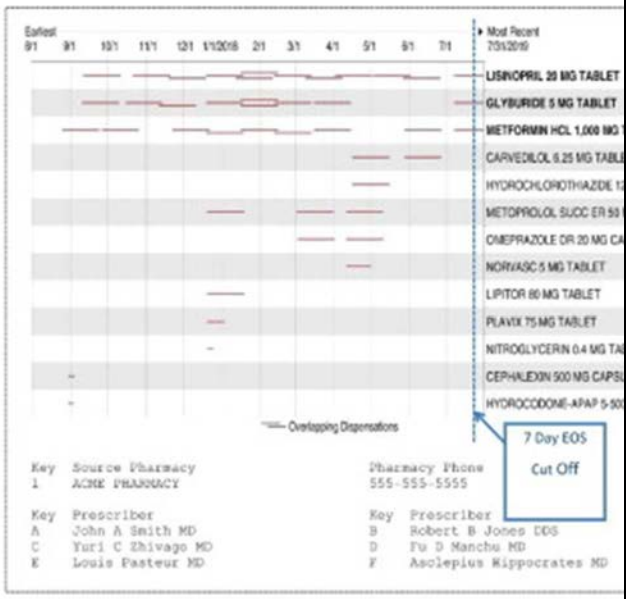
Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #3	General	Report is well written and clinically meaningful. While an abundance of research has been done to evaluate HIE, this report validates earlier systematic reviews which have found that there is insufficient evidence to determine the overall effectiveness of HIE or whether HIE has an impact on patient outcomes. Target population and key questions clearly stated. Unfortunately, there is insufficient evidence to fully address many of the key questions.	Thank you.
TEP Reviewer #3	General	: The report is well structured, well organized. I like the idea of a formal analytic framework based on Rasmussen's socio-technical system. Would be great if you could include a figure as an example of levels of analysis/research foci based on the findings of this report.	We added a figure based on Rasmussen's work.
Peer Reviewer #3	General	: I used the page numbers at the bottom of each page. Overall, the report is balanced and accurately reflects the state of HIE studies to date. I think the paper gave a good description of the challenge of doing the report and outlined those challenges. The analytical framework and questions are focused on the correct areas.	Thank you.
Peer Reviewer #3	General	Because of the reasons stated in the report, it is hard to make policy decisions based on the findings acrossed all the reports. However, it does give future studies some direction. It does give the reader an idea of the current state of HIE. The summary of facilitators and barriers were especailly helpful.	Thank you.

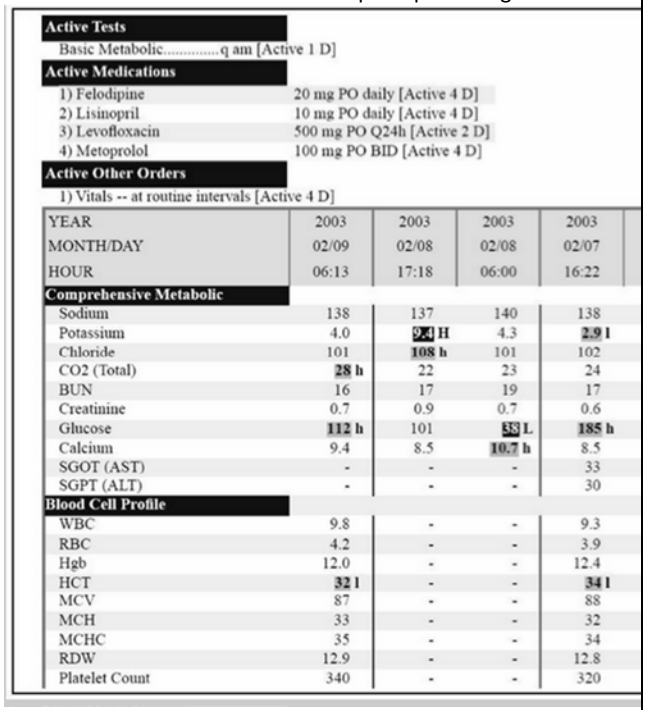
Commentator & Affiliation	Section	Comment	Response
TEP Reviewer #4	General	This is a truly excellent review which provides a very readable and valuable review covering a broad range of studies. The authors should be congratulated on dealing with such a disparate range of studies applying multiple methods in such an expert fashion. The methods applied are clearly described and executed. I would also note the very limited number of typographical errors given the size and complexity of the report, which is a feat in itself. I enjoyed reading the report. Preparation of an executive summary for such a vast body of research is immensely challenging and the authors have succeed in presenting an excellent overview. There are a few minor areas in the executive summary where considerable could be given to clarifying particular issues. While most of these areas are well addressed in the body of the report, some readers may not make it this far and thus it would be worthwhile considering some minor amendments to the summary	Thank you.
TEP Reviewer #4	General	Typographical issues P 20 line 33 was should be were Line 45 possible-wording – there was a reduced rate of test ordering increase… P 21 line 42 replace higher with greater P 68 line 17 ".. so that HIE usage because routine" because should be become? P74 dot point 3 It is not clear whether this result " ..HIE was used by between 30-58% of hospitals" relates to when HIE was available, or of all hospitals regardless of whether HIE was available. P 79 line 17 remove comma before positive impacts	All of these typos have been corrected.
Peer Reviewer #4	General	I commend the authors of this report for an exhaustive and well-documented literature review.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	General	It is possible that the goals of the report and the key questions that guided it were overly ambitious. The AHRQ defined as the goal of this report " to systematically identify and synthesize evidence on the extent to which HIE is effective in improving a variety of outcomes and determine if is is possible to say how much the impact varies by different approaches to HIE. The report also aims to identify evidence on use, usability and facilitator, barriers and sustainability indicators. (p 2, lines 45-51).	The goals of the report were ambitious, but we have used systematic review methodology, guided by technical experts, to achieve those goals to the extent that the published literature allows.
Peer Reviewer #4	General	This reviewer has three concerns with the manner in which the charge was addressed: 1) HIE was treated sometimes as a noun (an organization that facilitates transmission of electronic health data, perhaps by providing intermediary storage) and sometimes as a verb (the act of sharing information); 2) usability focused only on the end users' consumption of clinical data and did not address, explore or even document the contribution of data from a clinical site into an HIE process; and 3) the existence and use of the HIE was decontextalized; that is, there was little attention given in the report as to whether the studies that informed the report considered the local state of health information resources available to clinical users (although the authors did attempt to address this through evaluation of external validity).	As noted above, we have clarified HIE as verb vs. noun. We acknowledge that the literature is weak in assessing the state of local health IT and call for attention to this in future research.
Peer Reviewer #4	General	The report has general clinical relevance, in that it provides modest evidence of the presence of some type of an HIE on subsequent clinical service use. The challenge of demonstrating the clinical relevance of health information exchanges lies in characterizing the clinician-facing aspects of health information exchange in greater detail than was afforded by the studies available to the report writers.	We acknowledge this limitation and call for more attention to it in future research.
Peer Reviewer #4	General	It is disappointing that the report is written in an a theoretical manner. This decision is not documented and it almost forces the report to be a concatenation of observations rather than a systematic story about what is happening in HIE and why.	As already noted, we have applied systematic review of the scientific evidence methodology in this report, which means our analysis is based on published literature.
Peer Reviewer #4	General	Finally, although it is clear that this document is a heroic effort, there is a need for another round of copy-editing. There is a duplicate sentence on page 16 and there are noun-verb and tense discrepancies throughout.	The report has gone through copy editing and we have made these additional changes.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	General	The report is clearly written. The main points are clealy presented. I believe that the primary contribution to policy or practice decisions is to provide a foundation indicating a positive baseline of HIE work.	Thank you.
Peer Reviewer #4	General	It is not clear why the report did not make use of some of the recommendations provided in the section on "Future Research Needs" (Page 100). Adopting a more formal analytical framework and taxonomy would have provided an organizing framework for the over 100 studies enumerated here.	Our charge was to provide systematic review methodology and make suggestions for future research, which includes these recommendations.
Peer Reviewer #4	General	The call to conduct research regarding how to implement HIE is not sufficiently informed by the evidence summarized in this report. For example, it would seem that based on the findings here, studies of HIE should characterize the HIE organization in terms of governance, purpose, etc (see Tables 10 and 11) prior to examining for impact. In addition, studies should be explicit regarding the level of analysis.	We revised the future research section to be more specific and clear regarding what research is needed to fill in the gaps of this review.
Peer Reviewer #4	General	Calls for the use of complex adaptive systems theories to guide the work are acceptable but not actionable. One would presume (employing the complex adaptive systems framework) that HIEs are more of a process than a fixed entity. While that consideration is plausible, it is not supported by the evidence presented in this review.	We disagree, and note that HIE is a fluid area whose future is uncertain, due in part to the problems uncovered in this report.
Peer Reviewer #5	General	The basic material is here and well-organized, but some relationship between the type of HIE and the characteristics (time to access, consent requirement, richness and complexity of available data) should modulate the conclusion.	HIE implementations, and their description in the evaluative literature of them, are idiosyncratic, so a task like this is beyond the scope of the systematic review methodology of this report.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	General	Overall, I love this review. You have collected a tremendous amount of information. I like the overall organization and the way you have summarized the papers. But I have lots of detailed comments and suggestions, including about the categorization of HIEs, which did not find the right dimensions to emphasize and this might be due in part to a strict focus on quantitative papers that provided data relevant to your quest. A bit of a dive into papers that descried the HIEs might have shed better light on the distinctions among them. I had to dig out one of Frisse's descriptive papers to figure out that it is really a centralized system with segmented data. (Regenstrief did something similar to make the hospitals more comfortable, but it is definitely centralized not federated.) Also think there are opportunities to gather and focus the issues that you uncovered a bit more sharply. Overall, this is a very good review, full of rich detail, well organized and well written. Kudos to the authors. But think the report would benefit from some stronger summative opinions – What I took from it was that: Some HIEs have only minimal use. Further, one could predict the characteristics that would lead to high use versus low use, and the papers you summarized verify those predictions.	We agree that more details about HIE organizations and implementations would be valuable, but such information is not readily available in the published literature. As such, we call for a more detailed taxonomy of HIE that better defines the outcomes of future research.
Peer Reviewer #5	General	High use will come: 1) When the HIE carries a critical mass of data beyond what is available to the local EMR. a. My wager – any HIE that carried any three of: lab results, radiology reports, ECGs, cardia echoes, medication profiles, and discharge summaries for nearby health care systems would be loved and used heavily – unless it required too much hoop jumping to use.. 2) When provider time costs required to access the HIE data are low – seconds or less. Provider time costs will always be lower when: a. Staff do the accessing. b. The check in process triggers a request for the HIE to send a chunk of info about the newly-registered patient to the local EMR or to a local printer and staff attaches the report to the encounter document. Maybe	We agree with these recommendations to improve HIE but what is proposed here is a hypothesis that should guide future research.

Commentator & Affiliation	Section	Comment	Response
		also with push. However the description of push system was not clear to me. c. It could also be fast during a provider-initiated look up if the machines were quick and the data was well integrated across contributing organizations. 3) The data delivered is organized thoughtfully for easy digestion. a. For example, a dump of all filled prescriptions organized by dispensing data for the last year will be hard to digest. It would be a jumble of 50-100 records. Prescription data is most easily digested when, for example, it squeezed down to an active profile (see example in Figure 1).1  Figure 1. Medications Report. Dispensing of each medication over time. Each red, horizontal line represents a single new prescription or refill, and its length represents the calculated duration of the supply dispensed. We	

Commentator & Affiliation	Section	Comment	Response
		considered any medication with a duration line that crossed the blue dashed vertical line (end of supply is within 7 days of ED visit) to be a recent medication. The document lists the prescribers for each medication. This example patient had 6 different prescribers (fictitious names shown), 13 medications of which the first 3 were considered recent. This report is produced by the NLM/Health Level Seven server and is not the native report delivered by Surescripts.[1] b. Ideally the labs would be delivered as short flowsheets. See example report in Figure 2.[2]  **Active Tests** Basic Metabolic.....q am [Active 1 D] **Active Medications** 1) Felodipine 20 mg PO daily [Active 4 D] 2) Lisinopril 10 mg PO daily [Active 4 D] 3) Levofloxacin 500 mg PO Q24h [Active 2 D] 4) Metoprolol 100 mg PO BID [Active 4 D] **Active Other Orders** 1) Vitals -- at routine intervals [Active 4 D] YEAR 2003 2003 2003 2003 MONTH/DAY 02/09 02/08 02/08 02/07 HOUR 06:13 17:18 06:00 16:22 **Comprehensive Metabolic** Sodium 138 137 140 138 Potassium 4.0 9.4 H 4.3 2.9 l Chloride 101 108 h 101 102 CO2 (Total) 28 h 22 23 24 BUN 16 17 19 17 Creatinine 0.7 0.9 0.7 0.6 Glucose 112 h 101 33 L 185 h Calcium 9.4 8.5 10.7 h 8.5 SGOT (AST) - - - 33 SGPT (ALT) - - - 30 **Blood Cell Profile** WBC 9.8 - - 9.3 RBC 4.2 - - 3.9 Hgb 12.0 - - 12.4 HCT 32 l - - 34 l MCV 87 - - 88 MCH 33 - - 32 MCHC 35 - - 34 RDW 12.9 - - 12.8 Platelet Count 340 - - 320 Figure 2. Typical snippet from the new version of "Pocket Rounds" report.[2]	

Commentator & Affiliation	Section	Comment	Response
		4) When the consent requirements are not onerous. • HIPAA has never required consent for accessing clinical data required for care but access to HIEs for clinical care has often been constrained by extra steps and permission. • In some settings –e.g. emergency room -- it makes no sense to obstruct data flows that could be essential to good patient care. • No one would want to be operated on by a blindfolded surgeon, so would assume patients would not want to blindfold the treating internist. 5) When sufficient keys are available in the HIE to link to the current patient. • SS# is a great specifier.3 But many forces are constraining its availability so it is becoming less available. If it were encouraged, the last 4 digits of SS# might be almost as good when taken with other, more available keys. Studies are needed. • In stable populations, over modest durations (e.g. 1-2 years), the combination of phone #, birthdate, name, and zip code are probably pretty good. But when patients have to move a lot, or when they come from areas with high densities of some ethnic groups, names such as Li and Jose may repeat too much to be reliable identifiers.	

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	General	What makes an HIE? Don't understand what you mean by direct provider to provider communication. And in general, think you need a section that outlines and clarifies the distinction between different kinds of "HIEs." I think of HIEs as a system pre-arranged with a set of organizations and/or practices, at least some of whom share their data with others in the group. Some of the connection you describe sounded like encrypted email across practices– that does not assure any particular set of data is available to the community of providers, and I had not thought of that as an HIE. Not clear what spectrum of arrangements this report considers to be an HIE. But would help a lot to include some examples to compare and contrast with the classic HIE. Is it just encrypted email among providers? In summary, it would help if you could provide a clear definition of the different categories of what you think of as HIEs, what each can and cannot do (e.g., the richness of their data sets and the obstacles to access), and give examples. If you could then relate your categories to your data and conclusions, the report would be more instructive	We have clarified that we have adopted the ONC view of HIE, which in our view is accepted more generally than any other.
Peer Reviewer #5	General	Taxonomy of HIEs and how they provide data. The taxonomy of organization and methods of access for HIEs provided by the ONC (ref 13 page 14) is not clear and does not include all important dimensions. An expanded presentation with more distinctions early in the report would facilitate readers' digestion. For example, I was not sure of what directed exchange is: An email between two providers? A request from one provider to have the other send him/her some data? Are they referring to the historic method: ER calls a hospital or an office and asks them to send results? That is a well-traveled path, but would not have thought that was integral to, or part of, an HIE. Whatever it is, does not sound much different from query based exchange. And what is a consumer mediated exchange and does any such system exist? My understanding has been that consumer-based exchange depends upon widespread uses of PHRs, but that has not happened. So I am confused.	The ONC definition of HIE focuses more on functionality than architecture. We agree that a more detailed taxonomy is necessary and call for future research to develop this taxonomy and make sure it is applied by researchers going forward.

Commentator & Affiliation	Section	Comment	Response
		Page 49 talks about types of HIEs, but is really describing many different facets, including what kind of data, what kind of people are connected, whether they were opt in or opt out, and a little bit about the kind of connections (DIRECT to send cCDA) -- all useful and interesting – but does not distinguish or classify the spectrum of different cases. I think the spectrum runs from: a) Centralized – The centralized database with pre-unification (linking) of patients and use of a common code system across data sources for tests and reports) so that the HIE contains a unified patient record and the user can find all of a patient's data in one place. Access to such systems can be implemented as a lookup at providers' initiative or as a summary report triggered by the check-in system at the local care site to the HIE (Figures 1 and 2 were both be generated by this 2nd way). This automatic trigger that sends a request to the HIE, which then sends the report to the care site, eliminates "all" of the effort needed to access the mother lode. b) Distributed system with pre-standardized data – stored in databases systems, often called edge servers – at each data source and the HIE includes an associated master patient registry. The edge servers are located at the source system, but their database structure and coding may be standardized to various degrees. I think that the FDA's Mini Sentinel is constructed this way. These systems variously send data in a merged form or in separate chunks from one institution at a time. For HIEs, this distributed approach was the rage emphasized by the cognoscenti, but don't know that any that worked were built. c) Distributed with no edge system but a master patient registry. More problems in delivering timely results upon query.	

Commentator & Affiliation	Section	Comment	Response
		d) A set of independent systems which give access to a set of providers. But they have to access them one at a time for a given patient. These are often associated with a centralized master patient index that indicates which institution carries data for a given patient. e) Encrypted email – which provides a convenient way to deliver reports from hospital to doctor, patient, and between practices. A useful function but not sure that it equals an HIE. Would depend on how much and what kind of data is sent consistently. The report should clarify the categories of HIE it is talking about when it makes assertions. Not arguing for the exact categories I have listed, but at least 3-4 distinct kinds.	
Peer Reviewer #5	General	Separate focus is needed on the issue of patient matching: how it's done and whether automatic and whether users have to search within the master index file to find hospitals that might carry a patient and then look for the patient. If the process is slow or complicated, it will only be used in desperate circumstances. Much easier to just call the medical record room where the patient reports may have been.	We agree that continued research on patient matching is required.
Peer Reviewer #5	General	A parallel question about how much mapping of tests and reports is done by the central HIE. Well- organized, minimally redundant reports cannot be generated without some mapping and use of a common set of codes.	We agree with this.
Peer Reviewer #5	General	Last thought. The critique of sustainability of HIEs was unfair on two counts reported. The 5-year survival of all start-up businesses is about 10%. In that context, the 30% success sounds good. An HIE is an example of a network economy. The value of such systems increases with the mass of its contents, number of users and frequency of usage. It can take a long time for a network system to reach critical mass. But markets appreciate their value well before they become profitable (Twitter is a good example). It will probably take 5 more years and wider availability of standards before HIEs reach critical mass. So would not hang crepe too early	We agree with this sentiment but it is an opinion that is not based on the evidence we discovered.

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Peer Reviewer #5	General	So overall, think the final conclusions based on available published data have to be qualified by the fact that very few HIEs had a sufficient critical mass of data and integration to achieve the stated goal of widespread unified availability of patient data, and some had constraining consent requirements. So don't think the studies reflect enough experience with "full" HIEs to answer important policy questions. But does provide insight on how HIEs should be constructed to get better usage. The study would ideally be repeated later as standardization of data finally takes hold. (It is not until MU3 – scheduled for 2017) that all lab data within an EMR must use LOINC codes. There is some encouragement for coding the names of radiology reports with LOINC in MU3, but still no encouragement about any coding for other test results.	We agree, and in future research call for continued systematic review of the published literature.
TEP Reviewer #5	General	This is a timely review of evidence for HIE effectiveness and was done in an appropriate fashion given the variability in the literature regarding this topic. The authors do a good job of describing the limitations in the state of the literarture about evaluating outcomes of HIE's at this time.	Thank you.
TEP Reviewer #5	General	This report is well organized and written and will prove to be useful as it provides some framework for how to assess the likelihood of sucess of a new HIE project.	Thank you.
TEP Reviewer #5	General	The one challenge I see regarding how to keep this relevant will be the status of rapidly changing adoption,implentation or and optimization as well as the change in the technology sulutions being offered. This will change much faster than the poliy that will likely be derived from this project overall	Noted.
TEP Reviewer #5	General	In general - one place that could be strengthened would actually be in suggesting a more thourougn set of critera for future article writers as they prepare for the early evaluation of the design, implementation, and outcomes from HIE models that inevitably might be more easily enabled by adoption of new standards and technology in the future.	We agree, and have elaborated more details in our calls for a taxonomy that helps contextualize future research.

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Peer Reviewer #6	General	Report is very well organized and written. It includes many summary figures that enrich its clinical utility. One small weakness of the report is that the overall recommendations do not take into account the challenges of program evaluation. In this area, study design is often dictated by the goals of the program, and not the reverse. Therefore, for example, papers discussing cost-benefit, while limited in the scope of what they analyzed may be more useful (since they all show benefit) than described here.	We have added a statement and reference to the challenges of program evaluation in the introduction.
Peer Reviewer #6	General	It is possible that the report could have summarized the trends in the literature, as well as the conclusions based on the specifics of individual studies. This approach was most evident when talking about barriers, and least evident in the more quantifiable aspects of the evaluation, such as usability and sustainability.	Thank you. We have provided more details about the number of papers supporting themes related to barriers to use.
Peer Reviewer #7	General	Overall, this is a wide-ranging and well written report on an important topic. The authors have collected and assessed best published evidence about 7 key questions on health information exchange (HIE): effectiveness, harms, intermediate outcomes, level of use, usability, facilitator/barriers to use, facilitator/barriers to implementation, and sustainability. One conclusion is the limitations in the current evidence, with existing studies suffering from less than optimal study design and narrow scope. Another is that the evidence about the effect of HIE is mixed, with a certain amount of positive evidence supporting its effect in reducing certain types of healthcare utilization and improving certain quality of care metrics.	This is consistent with our conclusions.
Peer Reviewer #7	General	e. Minor wording: On page 20, the authors state that "HIE is only partially associated with the clinical outcome (i.e., many more factors go into clinical outcomes than the decision to consult an HIE…)." This awkward phrasing could be revised, for example, "HIE is only one of many potential influences on clinical outcomes…"	This has been changed in the Results section.
Peer Reviewer #7	General	This report is well structured, organized and usable.	Thank you.

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Peer Reviewer #8	General	I feel that to the best of the limits of the evidence provided this report is clinically meaningful. Good searching for the population information. Excellent use of the Key questions to structure the document.	Thank you.
Public Reviewer #2	General	vii "...health information exchange (HIE), the sharing of information across the boundaries of health care organizations." ES-1 "Health information exchange (HIE) is the sharing of electronic clinical data across organizations." p.1 "...health information exchange (HIE), which has been defined as the reliable and interoperable electronic sharing of clinical information among physicians, nurses, pharmacists, other health care providers and patients across the boundaries of health care institutions, health data repositories, states and other entities who are not within a single organization or among affiliated providers." The term "health information exchange" (HIE) is commonly used both as a noun and as a verb. ONC's attempt to restrict the definition of HIE to a verb and to introduce health information organization (HIO) as the noun variant of the term increased rather than reduced terminology ambiguity. Many of the 115 studies selected for the systematic review use HIE as a noun in their title, while the key questions restrict the term to the verb. Meanwhile, the draft review narrative casually shifts between HIE as noun or as verb. Here's an example: "Within organizations with HIE, the number of users or the number of visits in which the HIE was used was generally very low. The degree of usability of an HIE was associated with increased rates of use, but not with effectiveness outcomes. The most commonly cited barriers to HIE use were incomplete patient information, inefficient workflow, and poorly designed interface and update features." [p.vii]	We have clarified in the report that we view HIE as a verb or activity-based noun, and have revised the text thoroughly to reflect that.

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		It would be a service to the cause of "precision informatics" if the systematic review can address this noun/verb terminology ambiguity. RWMN notes that HIE the noun tends to correspond to a curated clinical data repository information architecture, while HIE the verb adapts to HIE services as clinical data supply chain as well as HIE services as a clinical data repository. RWMN also notes that a data supply chain answers the question a clinician asks about the immediate episode of care for an individual patient, while a repository is the right way to answer population health questions.	